Remarks/Arguments

In response to the Restriction Requirement, Applicants have elected, with traverse, claims drawn to nucleic acid-based methods of determining whether a human subject is at risk for developing obesity comprising the steps of obtaining a TBC1D1-encoding nucleic acid from said subject and detecting an alteration in said TBC1D1-encoding nucleic acid that is associated with a risk of developing obesity. However, Applicants respectfully assert that no serious burden would be imposed on the examiner to examine the claims of all three claim groups (I, II & III) together, since the gist of the disclosed invention is the discovery that specific products of the TBC1D1 gene are associated with an enhanced risk of obesity in humans.

While the claims of groups I & II may be classified into two different groups of diagnostic methods (nucleic acid-based methods and protein-based methods, respectively), the patentability of both groups of diagnostic methods revolves around the association of TBC1D1 protein variants with an increased risk of a subject developing obesity. Thus, Applicants respectfully assert that a single search (e.g., "TBC1D1 AND obesity") can be used to determine if relevant prior art exists that may preclude the allowance of both sets of claims in claim groups I & II.

Claim group III is drawn towards methods of screening for drug candidates useful in treating obesity, wherein said drug candidates alter a biological activity of TBC1D1. Thus, the novelty and nonobviousness of the subject matter in this claim group is also determined by the novelty and nonobviousness of the underlying association of variants of TBC1D1 with increased risk of obesity. Consequently, the same search proposed above for claim groups I & II (e.g., a search that address the association of TBC1D1 with obesity) could be used to assess the patentability of the claims in claim group III.

In view of the above, Applicants respectfully submit that the same searches would apply to all claims in all three claim groups, and thus, no serious burden would be imposed on the Examiner by examining all the pending claims together. Applicants note that as **required** by MPEP §803, "[i]f the search and examination of the entire application can be made without serious burden, the examiner **must** examine it on the merits, even though it includes claims to independent or distinct inventions." See MPEP 803, 8th Edition, 2nd Revision, May 2004, page 800-4 (emphasis added).

With regard to the secondary requirement for restriction made in Section 3 of the Restriction Requirement, wherein the Applicants are required to select between three specific nucleic acid or protein variants, Applicants respectfully assert that the requirement is based upon a fundamentally flawed allegation – namely, that the instant case deals with nucleotide sequences encoding "different" and "unrelated" proteins. Applicants maintain that the statement recited on lines 3 and 4 of page 3 that "[n]ucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another" is not relevant to the instant case, because the proteins in question are variants of the **same** protein that are most definitely **related** to one another. Applicants further maintain that one of average skill in the art, apprised of the instant invention, would reach this same conclusion, particularly since the three disclosed nucleic acid variants differ from "wild-type" by a single nucleotide out of 2022 nucleotides, and the disclosed protein variants differ by a single amino acid residue out of 674 amino acid residues. Further, to conclude that such variants are not related to wild type is preposterous, since every living geneticist or molecular biologist would agree that such variants arose directly from the wild type gene through mutation, and that the variants were, in essence, direct descendents of the wild type.

Regardless of semantic arguments about whether nucleic acids bearing single substitution mutations encode "different" and "unrelated" proteins, Applicants note that sequence-based searches of nucleotide sequences or amino acid sequences using modern search methods, and conducted with wild-type sequences, will reveal – in the very same search –the single nucleotide polymorphisms or substitution mutations known in the art. Hence a single search with the wild type sequence is sufficient to identify art that might disclose the three specific variants claimed.

Additionally, in 1996 the Commissioner of the USPTO proclaimed:

> "to further aid the biotechnology industry in protecting its intellectual property without creating an undue burden on the Office, the Commissioner has decided sua sponte to partially waive the requirements of 37 CFR § 1.141 et seq. and permit a reasonable number of such nucleotide sequences to be claimed in a single application.
>
> Accordingly, in most cases, up to ten (10) independent and distinct nucleotide sequences will be examined in a single application without restriction. It has been determined that normally ten sequences constitute

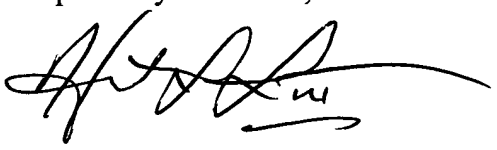
> a reasonable number for examination purposes. The PTO believes that allowing applicants to claim up to ten (10) independent and distinct nucleotide sequences in a single application will promote efficient, cost-effective examination of these types of applications. In addition to the specifically selected sequences, those sequences which are patentably indistinct from the selected sequences will also be examined. "
>
> [1192 OG 68 (11/1996)]

To the best of Applicants' knowledge, this proclamation has not been reversed, altered, or revoked. Hence, the Applicants respectfully request that the directives of this proclamation be followed, and all three variants be examined in the instant case.

In conclusion, Applicants respectfully request that all pending claims be examined on their merits, and the secondary restriction requirement be withdrawn so that the association of the three disclosed nucleic acid and protein variants with an increased risk of obesity can be examined simultaneously.

It is not believed that any time extension or fees are required with this response. If this is incorrect, an extension of time as deemed necessary is hereby requested, and the Commissioner is hereby authorized to charge any appropriate fees or deficiency or credit any over payment to Deposit Account no. **50-1627**.

Respectfully submitted,



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